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Treatment of Trypanosomiasis With p-Arsenosphenylbutyric Acid

A List of Public Health Service Publications—1945



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Public Health Reports

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THE TREATMENT OF TRYPANOSOMIASIS WITH p-ARSENOSOPHENYLBUTYRIC ACID

I. RESULTS IN 319 CASES OF EARLY *TRYPANOSOMA* *GAMBIENSE* INFECTIONS¹

By HARRY EAGLE, Senior Surgeon, United States Public Health Service

Unlike most acid-substituted phenyl arsenoxides (1), (2), γ -(p-arsenosophenyl) butyric acid is an active trypanocidal agent. Its synthesis and chemical properties (3), its toxicity (4), and its marked therapeutic activity in experimental *Trypanosoma equiperdum* infections of mice and rabbits (1) have been described in previous communications from this laboratory (table 1). In further experimental studies, van Hoof, Henrard, and Peel (5), working with *T. gambiense*, and Davey and Scott (6) working with both *T. equiperdum* and *Trypanosoma rhodesiense*, found the trypanosomal species pathogenic for man to be equally susceptible to treatment.

The initial results obtained in the treatment of human cases (7) suggested that it might be possible to cure early cases within 2 weeks or less, and with relative freedom from toxic complications. Particular interest attached to the fact that the compound was active both *in vitro* and *in vivo* against a typical "arsenic-fast" strain of *T. equiperdum* (8), a property confirmed by van Hoof, Henrard, and Peel (5) with a similarly resistant strain of *T. gambiense* tested in both animals and man.

The present communication will deal with 319 human cases of *T. gambiense* infection treated with p-arsenosophenylbutyric acid in the early stages of the disease, before the central nervous system had become involved. These cases have now been followed for sufficient periods of time to permit a reasonably accurate appraisal of the tox-

¹ From the Venereal Disease Research and Postgraduate Training Center of the U. S. Public Health Service, Johns Hopkins Hospital, Baltimore 5, Md., with the active collaboration of the Sleeping Sickness Services of the Belgian Congo, French Equatorial Africa, French West Africa, the Gold Coast, Nigeria, and the Firestone Plantation in Liberia.

TABLE 1.—*Experimental data with respect to toxicity of p-arsenosphenylbutyric acid and therapeutic efficacy in experimental T. equiperdum infections*¹

A. TOXICITY					
Number of injections	Animal species	Route of administration	Maximal tolerated dose (LD ₅₀) (mg./kg.)	LD ₅₀ (mg./kg.)	LD ₉₀ (mg./kg.)
Single injection.....	Mice.....	Intraperitoneal.....	26	33	50
	Rabbits.....	Intravenous.....	2.8	4.5	7.5
	Dogs.....	Intravenous.....		7.5±	
B. THERAPEUTIC EFFICACY					
Animal species	Method of treatment	Total curative dose, mg./kg.		"Chemotherapeutic index"	
		CD ₅₀	CD ₉₀	MTD ² CD ₉₀	LD ₅₀ ³ CD ₅₀
Mice.....	Single injection, intraperitoneal.....	1.6	3.4	7.6	20.5
Rabbits.....	Four daily injections, intravenous.....	3.6	6.0	1.3	4.5

¹ After (1).² Maximal tolerated dose.

Dose which cures 90 percent.

³ Dose which kills 50 percent.

Dose which cures 50 percent.

icity and therapeutic efficacy of the compound, as well as the optimum method for its administration. Subsequent papers will consider the far more difficult therapeutic problem presented by advanced cases, with definite involvement of the central nervous system, as well as various types of animal trypanosomiasis, studies which are now in progress.

As is indicated in table 2, the data here reported represent a collaborative effort by the Sleeping Sickness Services of the Belgian Congo, French Equatorial Africa, French West Africa, the Gold Coast, Nigeria, and the Firestone Plantation in Liberia. Some of the cases included in the present report were treated during the writer's first trip to West Africa, in the summer and fall of 1944

TABLE 2.—*Clinics participating in the study on the therapeutic efficacy of p-arsenosphenylbutyric acid in human trypanosomiasis*

Colony	Area of treatment	Number of cases included in present report	Collaborating physicians
Belgian Congo.....	Leopoldville, Mikungu.....	47	Gen. L. van Hoof, B. Rodjstvensky, Scaillet.
French Equatorial Africa.....	Brazzaville.....	41	Col. Ceccaldi.
French West Africa.....	Bobodioulasso.....	6	Lt. Col. L. Nodenot, Col. C. LeRouzic.
Gold Coast.....	Kintampo, Ejura.....	22	G. Saunders, Brig. G. M. Findlay.
Liberia.....	Firestone.....	10	R. H. Kinderman.
Nigeria.....	Ungwa Rimi, Zagon, Rigachikun.....	193	J. L. McLetchie, C. Hollins, K. E. U. Ground.

(7); the majority were treated subsequently by the several sleeping sickness services, and their histories obtained during a second visit in the summer and fall of 1945. The number of physicians participating in the study precludes their inclusion as coauthors; but the study would obviously have been impossible without their continuing interest and cooperation. With the exceptions discussed in the text, consistent results were obtained in the various colonies. The conclusions here drawn, based on the composite experience, thus differ only in detail from the individual appraisal of the several medical services.

Methods and Materials

Drug

The free p-arsenosphenylbutyric acid is a water-insoluble white compound which dissolves in alkali to form a yellowish solution of the highly soluble sodium salt. The drug was first packaged in glass-sealed ampules as a sterile 2-percent solution adjusted to pH 7.0. After about 12 months, apparently due to an interaction between the sodium salt and an inferior, perhaps acid-treated glass, the pH had dropped to 6.0, and approximately 7 percent of the compound precipitated from the solution as the free acid. Subsequently, the drug was packaged as a stable dry powder in sterile rubber-stoppered vials, each containing 200 mg. of the acid in the form of the sodium salt. This dissolved readily on the addition of 10 cc. of water to form the 2-percent solution usually injected. There is reason to believe that with properly selected glassware, solutions at pH 7.0 to 8.0 will remain stable in glass-sealed ampules.

Method of Administration

Most of the patients received approximately 0.4 mg. per kg. per injection. In a man of 60 kg. this unit dose was 24 mg., injected as 1.2 cc. of the 2-percent solution. In some clinics, it was found more convenient to use a 0.4-percent solution (4 mg. per cc.) in which case the 24-mg. dose for a man weighing 60 kg. was 6 cc. This average dose of 0.4 mg./kg. was $\frac{1}{2}$ of the maximum tolerated dose in rabbits, $\frac{1}{65}$ of the maximum tolerated dose in mice, and promised to afford a reasonable margin of safety (table 1). As is discussed in the text, in one small series of patients, five times that dosage level was administered daily for 8 days, with no demonstrable toxic reaction.

Almost all the patients were injected intravenously. A total of at least 12 patients were, however, injected intramuscularly (gluteal muscles) through the entire course of treatment, with either no reaction, or transitory discomfort at the site of injection.² The two modes

² The relative freedom from local reaction to this acid-substituted arsenoxide, in contrast to the marked inflammatory reaction following the intramuscular injection of, e. g., neoarsphenamine or mapharsen, is probably referable to the demonstrated lack of affinity between such acid-substituted arsenoxides and mammalian tissue cells (2), (16).

of administration proved equally effective therapeutically, and they are not distinguished in the text.

In order to determine the optimum amount and schedule of treatment, the number of injections was deliberately varied from 7 to 21, and their frequency similarly varied from twice weekly to once daily.

Selection of Patients

The clinical material was not selected with respect to either age or sex. All were natives of widely differing racial stocks. Sixty percent were males. Nine percent were less than 10 years of age, 25 percent were in the 10 to 19 year age group, 65 percent were 20 to 40, and 1.5 percent were 50 years or older. Since the therapeutic results were independent of age and sex, these subgroups are not distinguished in the text.

Fifteen cases treated as early infections are not included in the 319 analyzed. Three died of intercurrent infections (dysentery, cerebrospinal fever, and an unidentified disease) not related to the trypanosomiasis; in 2 no record had been kept of dosage; and in 10 there were no data as to the microscopic or spinal fluid findings on which the diagnosis of trypanosomiasis had been based.

In identifying the cases as "early," i. e., without demonstrable involvement of the central nervous system, the clinical history as to the duration of the infection proved wholly unreliable, as did either the external appearance of the patient or the subjective symptomatology. The clinical material here included therefore comprised 221 cases in whom either the blood, cervical lymph nodes, or both, were shown to harbor trypanosomes, and whose cerebrospinal fluid was normal. Unfortunately, the criteria of a "normal" fluid varied considerably between the various treatment centers. For the purposes of the present study, any patient with less than 10 cells per cubic millimeter, and less than 25 mg. of protein per 100 cc., was arbitrarily adjudged to fall into the "early" group, with a normal fluid; patients with 10 to 20 cells per cubic millimeter were included only if the spinal fluid protein was less than 20 mg. percent; and patients with more than 20 cells were excluded. There were 98 additional cases in whom lymph nodes, blood, or both were positive, who seemed in good clinical condition, and gave no history of a long-standing infection, but who did not have a spinal puncture prior to treatment. It is obvious that a small if indeterminate proportion of these quasi-early cases would have been discovered to have an altered spinal fluid, and thus, asymptomatic central nervous system involvement. For that reason, this group is not comparable to the other 221 cases, and is considered separately in the text.

Observation of Patients and Criteria of Treatment Failure

Patients were re-examined at varying periods after the completion of treatment, with particular reference to (a) the presence or absence of trypanosomes in the blood (wet and dry films) and cervical lymph nodes; (b) the cerebrospinal fluid findings; and (c) general clinical condition. The presence of trypanosomes, or abnormal spinal fluid findings, were taken as *prima facie* evidence of treatment failure. More than 80 percent of the patients had a spinal puncture at the time of the last observation indicated in table 6.

There were wide differences among the several medical services as to the degree of change in the spinal fluid findings to be considered indicative of pathologic involvement, and thus, of treatment failure. As ordinarily practiced, a spinal fluid cell count in which one actually scrutinizes no more than 1 mm.³ of fluid provides a total count with a large statistical error. Thus, an observed count of, e. g., 6 per cubic millimeter, may correspond to an actual count as low as 3, or as high as 12. Under such circumstances, one may properly question the validity of adjudging a case a treatment failure because the cell count had apparently changed from 4 to 8 or even 12. Even if that increase were real rather than apparent, normal variations in the spinal fluid cell count in the same individual are not inconsiderable, and render small changes suspect.

Similarly, in the determination of spinal fluid protein, most of the medical services in Africa use the method of Sicard and Canteloube (cf. (9)). Although it is a simple procedure admirably adapted to use in the field, its accuracy at levels less than 25 mg. percent leaves much to be desired. Even if the results could be taken at face value, there is so much normal variation in spinal fluid protein content that an isolated observation of e. g., 27 mg. percent may have little significance.

Several actual cases which illustrate the error which may be introduced by too hasty an interpretation of the spinal fluid findings are summarized in table 3. Few physicians responsible for the medical care of sleeping sickness would have hesitated to adjudge most, if not all, of these cases as treatment failures, yet all five proved to have a normal fluid when retested months later, without intervening treatment; and they have remained clinically well to the time of the last observation.

In view of the foregoing considerations, 13 cases which were adjudged treatment failures by the attending physician on the basis of minimal changes in the cerebrospinal fluid were not considered as such in the following analysis. The laboratory data in these cases

TABLE 3.—Cases illustrating the fact that even significant alteration in the spinal fluid observed after the completion of treatment for early trypanosomiasis do not necessarily signify treatment failure.

Case No.	Treatment		Spinal fluid findings				
	Total mg./kg.	Date of completion	Date	Cells per cu. mm.	Trypanosomes	Protein content, mg. (percent)	Globulin
L-77	3.9	1943 Dec. 29	Nov. 23, 1943	11	0	(?) 40	0
			Jan. 11, 1944	7	0	22	0
			Apr. 18, 1944	59	0	29	0
			Aug. 22, 1944	8	0	22	0
			Mar. 13, 1945	4	0	22	0
L-94	4.0	1944 Mar. 22	Feb. 22, 1944	9	0	22	0
			Apr. 4, 1944	22	0	40	0
			May 30, 1944	27	0	22	0
			July 12, 1944	5	0	18	0
			Sept. 11, 1945	8	0	22	0
L-130	3.6	Sept. 11	Aug. 1, 1944	11	0	18	0
			Sept. 19, 1944	12	0	56	++
			Dec. 5, 1944	9	0	22	0
N-754	5.1	Oct. 11	Mar. 11, 1945	16	-----	Pandy and neg.	Ross-Jones
			Sept. 3, 1945	8	-----	21	-----
N-773	5.5	Oct. 30	Mar. 12, 1945	135	-----	Pandy ±; neg.	Ross-Jones
			Sept. 3, 1945	5	-----	-----	-----

TABLE 4.—Cases in present series in which minor changes in the spinal fluid cell count or protein content observed after the completion of treatment were adjudged insufficient to establish diagnosis of treatment failure (cf. data of table 3)

Case No.	Treatment		Spinal fluid findings				
	Total, mg./kg.	Date of completion	Date	Cells per cu. mm.	Trypanosomes	Protein content, mg. percent	Globulin
B-29	2.8	Jan. 3, 1944	1944 Dec. 22, 1944	12	0	26	-----
			Mar. 12, 1945	17	0	21	-----
B-50	5.6	Feb. 6, 1945	Jan. 22, 1945	2	0	22	-----
			Mar. 16, 1945	10	0	20	-----
B-54	5.6	Feb. 12, 1945	Jan. 29, 1945	2	0	22	-----
			Apr. 27, 1945	12	0	22	-----
B-58	8.0	Feb. 26, 1945	Feb. 6, 1945	8	0	24	-----
			June 1, 1945	11	0	27	-----
B-60	8.0	Feb. 27, 1945	Feb. 7, 1945	3	0	24	-----
			Mar. 19, 1945	3	0	29	-----
B-63	4.4	Feb. 26, 1945	Feb. 15, 1945	2	0	22	-----
			Mar. 19, 1945	6	0	30	-----
M-45	5.7	Mar. 8, 1945	Feb. 22, 1945	8	0	22	0
			Apr. 9, 1945	10	0	22	0
M-47	4.7	Mar. 8, 1945	Feb. 22, 1945	8	0	24	0
			Apr. 9, 1945	12	0	22	0
M-96	3.0	Apr. 12, 1945	Mar. 30, 1945	3	0	12	0
			May 8, 1945	3	0	15	0
M-100	5.6	Apr. 27, 1945	July 24, 1945	12	0	10	0
			Apr. 10, 1945	4	0	20	0
M-101	5.6	Apr. 27, 1945	May 28, 1945	8	0	22	0
			Apr. 10, 1945	2	0	22	0
M-102	5.4	Apr. 27, 1945	May 28, 1945	7	0	22	0
			Apr. 10, 1945	2	0	15	0
M-126	6.0	Aug. 6, 1945	May 28, 1945	6	0	20	0
			July 20, 1945	8	0	22	0
			Sept. 6, 1945	12	0	22	0

are given in table 4, and have been held insufficient to establish the diagnosis of relapse. Indeed, on the basis of the data of table 3, one may properly question the significance of far more pronounced changes in the spinal fluid, unless confirmed by a repeat lumbar puncture 2 to 4 months later.

Calculation of Percentages of Cure and Treatment Failure

The percentage of treatment failure given in tables 6 and 7 was obtained by relating the number of observed failures to the total number of cases treated. This is clearly a minimum figure, since additional relapses will undoubtedly be discovered on longer observation (cf. page 1028). The small number of cases in each group, particularly in the longer observation periods, did not justify the calculation of the cumulative percentage of treatment failure (10). It is, however, estimated that the cumulative percentage of treatment failure will be approximately half again as large as those indicated in table 6.

Clinical Results

Rate of Disappearance of Organisms from Blood and Lymph Nodes After Treatment With p-Arsenosophenylbutyric Acid

Eighty-nine patients with trypanosome-positive cervical lymph nodes were re-examined at varying intervals after a single injection of p-arsenosophenylbutyric acid at 0.3 to 0.6 mg. per kg. As is shown in table 5, 88 percent of 25 tested were negative 30 minutes after treatment, 96 percent of 23 tested were negative 45 minutes after treatment, and 91 percent of 11 tested were negative 1 hour after treatment. Those still harboring organisms at the time of the first examination were regularly negative when retested $\frac{1}{2}$ to 1 hour later.

Seven of these 89 patients had been injected intramuscularly rather than intravenously. In 6, organisms had disappeared from the nodes within $\frac{1}{2}$ hour after the first injection; the seventh was positive $1\frac{1}{4}$ hours after the injection, but negative after 2 hours.

TABLE 5.—*The rate of disappearance of T. gambiense from the cervical lymph nodes after a single injection of p-arsenosophenylbutyric acid at 0.3 to 0.6 mg. per kg.*¹

Time between treatment and lymph node puncture	30 minutes	45 minutes	60 minutes	6 hours	Controls (untreated)
Number patients tested	25	23	11	30	16
Number negative	22	22	10	29	2
Number positive ²	3	1	1	1	14

¹ A total of 89 patients were injected and tested at the varying intervals indicated in the table. Of these, 7 were injected intramuscularly rather than intravenously. Six of these were negative when first tested, 30 minutes after the injections. In 22 patients the blood film also contained demonstrable organisms; in all, the blood became negative simultaneously with the lymph node.

² In the 4 patients with positive lymph nodes 30 or 60 minutes after treatment, organisms had disappeared on re-examination $\frac{1}{2}$ to 1 hour later. The case still positive 6 hours after treatment (cf. text) was negative the following morning.

Although 1 of 30 patients examined 6 hours after treatment was still positive at that time, the particular patient was an infant who received only 0.3 cc. of solution, and there may be some question as to the dose actually injected. His gland was negative when re-examined 24 hours after treatment.

Of the 89 patients in the test group, 22 demonstrated trypanosomes in the blood as well. In all 22, the blood had also become negative when trypanosomes had disappeared from the node. In 3 other patients with a positive blood film, but with negative lymph nodes, organisms had disappeared from the blood 30 to 60 minutes after the first treatment.

The rapid disappearance of trypanosomes from the blood and nodes after the injection of a single small dose of p-arsenosophenylbutyric acid is consistent with the marked trypanocidal action of the drug *in vitro*. Depending on the concentration of organisms, dilutions of 1:1,000,000 to 1:20,000,000 had been found to immobilize the organisms in 2 to 4 hours at room temperature, and even higher dilutions were effective in 24 hours (1), (2). These dilutions are of the same order of magnitude as those attained in the body fluids after the injection of 0.4 mg. per kg. body weight.

Only one patient proved to be relatively resistant to the drug. This 30-year-old male (L-146) relapsed (blood film positive) 8 months after completing an adequate course of treatment during which he received a total of 8 mg. per kg. When he was originally treated, organisms had disappeared from the cervical lymph nodes 30 minutes after the first injection of 0.47 mg. per kg. On retreatment, however, organisms disappeared from the blood only after 2 injections of 0.5 mg. per kg. each.

The previously demonstrated activity of the p-arsenosophenylbutyric acid against "arsenic-fast" strains of trypanosomes was confirmed in at least one case of the present series (case L-130 of Dr. L. van Hoof). A 27-year-old male with a trypanosome-positive cervical lymph node was treated with a single massive injection of 6 gm. of tryparsamide on August 8, 1944. On August 10 and again on August 14 persistent motile trypanosomes were demonstrated in the node by puncture. On August 30 he was injected intravenously with 30 mg. of p-arsenosophenylbutyric acid (0.5 mg. per kg.). The lymph node was negative when punctured the next day, and remained negative thereafter. The patient received 6 treatments to a total of 3.6 mg. per kg., and was well when last seen (June 6, 1945).

Toxic Reactions and Maximal Tolerated Dose in Man

The 319 cases included in the present report received a total of approximately 4,000 injections, with relatively few immediate or

delayed toxic reactions. The characteristic nausea-vomiting reaction so often observed after the injection of arsphenamines or "mapharsen" was conspicuously uncommon, occurring after less than 1 percent of the injections. Extravasations caused some local discomfort, but less than that observed after mapharsen. Twelve patients were injected intramuscularly, with either no reaction or transitory discomfort at the site of injection, and without further complication. The drug may therefore be injected intramuscularly in infants or obese patients in whom intravenous injection is not feasible.

One patient (UR-739) developed urticaria of the face within 30 minutes of the first injection, at 0.45 mg. per kg. This disappeared with no further complications, and there were no reactions to the second or subsequent injections. A second patient (UR-816) developed a painless jaundice after having received a total of 4.7 mg. per kg. in 12 injections over a period of 36 days. This cleared without further complications.

Two patients in the present series of 319 died within a week after the completion of treatment. One of these (UR-766) was not seen by a physician, and the cause of death remains obscure. The second case (B-57) was suspected of being a case of arsenical poisoning, but clinical and laboratory details were meager and inconclusive. Both cases were adults who had received a relatively small amount of treatment (total of 3.5 mg. per kg., at 0.4 mg. per kg. per injection).

Most of the patients received approximately 0.4 mg. per kg. per injection, repeated as often as once daily for as many as 23 injections. As is indicated in table 1, this is $\frac{1}{65}$ of the maximal tolerated dose on a single injection (intraperitoneal) in mice, $\frac{1}{7}$ of the maximal tolerated dose (intravenous) in rabbits, and $\frac{1}{19}$ of the single LD₅₀ (intravenous) in dogs.

Four patients were injected intravenously at 1.1 to 1.5 mg. per kg., and that same dose was repeated 2 hours later. This total of 2.2 to 3 mg. per kg. was seven to eight times the average single dose used in man, approximately half the maximum tolerated dose in dogs, and approximately equal to the maximum tolerated dose in rabbits. In none of the four patients was there an immediate toxic reaction or subjective discomfort, and they remained well for the remainder of the observation period. An error in dosage provided an even more rigorous test of the toxicity of the compound in man. A group of seven patients was injected in error with approximately 2 mg. per kg. This dose, five times the average injection, was repeated daily for periods varying between 5 and 10 days. There were no immediate or delayed toxic reactions in any of the seven patients.

It follows that cases of early trypanosomiasis can be treated by daily injections of p-arsenosophenylbutyric acid at 0.5 mg. per kg.,

and probably at 1 mg. per kg., with relative freedom from immediate or delayed toxic effects.

End Results of Treatment: The Minimal Curative Dose

In table 6, 199 cases known to have had a normal spinal fluid before treatment have been arranged vertically in four groups according to the total amount of p-arsenosphenylbutyric acid received in the course of treatment. Each group has been subdivided horizontally according to the length of time for which the patients have now been under observation. Since only 27 percent of the cases have been followed for 6 months or longer, additional failures will undoubtedly

TABLE 6.—Results in early trypanosomiasis in relation to amount of treatment received

Total treatment with p-arsenosphenylbutyric acid, mg./kg.		Observation period, months							Totals	Failures to date (percent)	Apparent cures to date (percent)
		<2	2-4	4-6	6-9	9-12	12-18	18			
<3.5	Number patients followed	21	11	7	3	1			43	26	74
	Number failures	5	5	1					11		
3.5-4.9	Number patients followed	4	2	2	16	4	2	1	31	10	90
	Number failures				3				3		
5.0-6.4	Number patients followed	15	4	9	8	1			37	8	92
	Number failures	1		1	1				3		
≥6.5	Number patients followed	11	18	39	5	15			88	5	95
	Number failures		1	2		1			4		

¹ In a group of 22 patients treated at this dosage in a single clinic, there were 9 failures (41 percent). As is discussed in the text, this anomalous result, coupled with the fact that 6 of the 9 failures were among the first patients there treated, strongly suggests a systematic error in dosage, a possibility in which the attending physician concurs. This group has been omitted from the table.

be encountered with longer observation. However, present experience indicates that treatment failures are encountered at a diminishing rate³ after the first 6 months; and the conclusions reached on the basis of the data now available will probably not be appreciably modified by further experience. The error introduced by not calculating the percentage of treatment failure on a cumulative basis has been discussed on page 1025.

1. Of the 43 patients who received a total of less than 3.5 mg. per kg. of drug, 6 have since shown organisms in the blood or lymph nodes, and 5 others had laboratory evidence of central nervous system involvement, a total relapse rate of 26 percent. Thirty-two (74 percent) remain well at the present writing.

2. Of the 31 patients who received a total of 3.5 to 4.9 mg. per kg.,

³ Most of the failures listed in the 6 to 9 month period were observed in patients then seen for the first time since the completion of treatment. It is probable that some of these would have been apparent had the patient been seen earlier, for instance, 3 months after treatment.

three have relapsed, all with altered cerebrospinal fluid, and 28 (90 percent) have remained well to date.

3. Of a total of 59 patients who received 5.0 to 6.4 mg. per kg., 12 were adjudged treatment failures, 6 with a positive blood film and 6 with alterations in the spinal fluid. This paradoxical result was referable to a single small series of 22 patients treated in a single clinic, no less than 9 of whom (41 percent) relapsed. Six of these relapses were among the first patients there treated. The possibility must be considered, and was seriously entertained by the physician in charge, of a systematic error in dosage with a new and unfamiliar preparation. If this group of 22 patients is omitted from consideration, among 37 patients who received a total of 5 to 6.4 mg. per kg., there have been 3 failures (8 percent), and 92 percent of the cases have remained well.

4. Eighty-eight patients received 6.5 mg. per kg. or more of the compound. To date, there have been four failures (5 percent) in this group, and 84 (95 percent) remain well. It is to be emphasized that almost 60 percent of this most favorable series has been followed for 4 months or more since the completion of treatment.

In considering those results, it is to be noted that the 11 treatment failures observed in 43 cases receiving less than 3.5 mg. per kg. were definite, comprising 6 cases with positive blood smears or lymph nodes, and 5 with indubitable central nervous system involvement. On the other hand, of the 10 treatment failures observed in 156 cases⁴ treated at dosages greater than 3.5 mg. per kg. (6.5 percent), in five the objective evidence for relapse consisted solely of an increased spinal fluid cell count (14, 24, 26, 28, and 30 per cubic millimeter), the protein content remaining normal or slightly elevated, and in no case exceeding 30 mg. percent. The lymph nodes and blood in those cases contained no demonstrative organisms, and the patients remained objectively and subjectively well. In one of these cases, the cell count had remained 22 to 26 per cubic millimeter for a period of 6 months. There is thus a possibility that at least some of these patients had not actually relapsed.

Results qualitatively similar to the foregoing were obtained in a second series of 98 patients, considered as early infections despite the fact that spinal puncture was not performed before treatment (table 7). This group therefore included an indeterminate number of cases with asymptomatic central nervous system involvement at the time of treatment (see page 1022). In the 47 such patients treated at 3.5 to 4.9 mg. per kg. there was one failure, a relapse rate of 2 percent, and an apparent cure rate of 98 percent. Thirty-seven of these patients have now been followed for periods of 6 to 12 months after

⁴ Omitting a single series of 22 cases in whom anomalous results were obtained perhaps referable to an error in dosage (page 1025).

the completion of treatment, and it is unlikely that a significant number will relapse with longer observation. There was one failure also in 17 cases treated at 5 to 6.5 mg. per kg. Paradoxically, there were no less than five failures in 32 cases treated with more than 6.5 mg. per kg. These supposed treatment failures almost certainly included some cases with central nervous system involvement prior to the beginning of treatment. It is significant that all of the apparent relapses in this series involved alterations in the spinal fluid; while in the known early cases (table 6) 7 of 21 actual or suspected treatment failures were detected by the reappearance of trypanosomes in the blood and glands, with no demonstrable involvement of the central nervous

TABLE 7.—Results in 98 putative cases of early trypanosomiasis (spinal puncture not performed before treatment)

Total treatment with p-arsenosophenylbutyric acid, mg./kg.		Observation periods, months					Totals	Failures to date (per-cent)	Apparent cures to date (per-cent)
		<2	2-4	4-6	6-9	9-12			
<3.5	(Number patients followed					2	2		
	(Number failures					0	0		
3.5-4.9	(Number patients followed	1	1	8	16	21	47	2	98
	(Number failures			1			1		
5.0-6.4	(Number patients followed	1	1		5	10	17	6	94
	(Number failures					1	1		
≥6.5	(Number patients followed	5	1	8	18		32	16(?)	84
	(Number failures			4	1		5		

system. This suggests that in at least some of the patients under discussion, the central nervous system may already have been involved at the time of treatment.

In summary, it seems clear from the foregoing considerations and the data of tables 6 and 7 that more than 90 percent of early *T. gambiense* infections can be cured by relatively small amounts of p-arsenosophenylbutyric acid, on the order of 6 to 7 mg. per kg., or a total of 360 to 420 mg. of drug in a man weighing 60 kilograms.

It is of interest to compare this curative dose in man with that observed in experimental animals with this and other species of trypanosome (table 8).

The Optimum Method of Treatment: Size of Individual Dose, Frequency of Injection, and Total Duration of Treatment

Of 156 known early cases of trypanosomiasis treated with a total of 3.5 mg. per kg. or more, 146 have remained well to date. If one includes the cases considered as early, but without information as to the spinal fluid findings, there were 252 patients in this category, of whom 235 (93 percent) remain well. Although these cases received comparable total amounts of the drug, the method of administration varied

within wide limits. The majority were given approximately 0.4 mg. per kg. at each injection, but some received as little as 0.25, and others as much as 2 mg. per kg. The total number of injections varied similarly from 3 to 23. Some patients were injected weekly or every 5 days, some twice weekly, some three times weekly, some daily, and some at irregular intervals. The total duration of treatment was from 4 to as long as 70 days. Within these limits of variation the factor determining therapeutic efficiency was solely the total amount of treatment received. Neither the size of the individual dose, nor the frequency of injection demonstrably affected the end results of treatment.

TABLE 8.—The curative dose of *p*-arsenosophenylbutyric acid in a variety of trypanosomal infections

Trypanosomal species	Animal species	Curative dose (CD ₅₀) of <i>p</i> -arsenosophenylbutyric acid, mg./kg.	Observer
<i>T. equiperdum</i>	Mice	3.4	Eagle, Hogan, Doak and Steinman (1)
		Arsenic-"resistant" strain equally susceptible.	Eagle and Magnuson (8)
		6.8±	Davey and Scott (6)
	Rabbits	6.0	Eagle, Hogan, Doak and Steinman (1)
<i>T. gambiense</i>	Guinea pigs	4.0	van Hoof, Henrard and Peel (5)
	Man	Arsenic-"resistant" strain equally susceptible. 6 to 7	Eagle.
<i>T. rhodesiense</i>	Mice	>3.4	Davey and Scott (6)
		<6.8	
<i>T. cruzi</i>	Rats	Temporary disappearance of organisms from blood after injections of 2 mg./kg.; animals not cured by 5 daily injections at that level.	Johnson (15)
	Mice	No effect with 6.8 mg./kg.	Davey and Scott (6)
<i>T. congolense</i>	Mice	No effect with 30 mg./kg.	Browning (11)
		No effect with 6.8 mg./kg.	Davey and Scott (6)
<i>T. evansi</i>	Mules and horses	Four of 9 animals still negative 2 weeks after receiving 6 injections at 1.25 mg./kg. each, given every other day. Less intensive treatment regularly ineffective.	Cordy and Kelser (12)

A similar relationship has already been observed in the treatment of syphilis with arsenicals, both in animals and in man. The curative dose of 3-amino-4-hydroxyphenylarsenoxide (mapharsen, clorarsen, and their analogues) in rabbits was identical, whether administered as a single dose within 15 seconds, or distributed over a period of 6 months (13); and in man also, total dosages of 1,500 mg. had the same effect whether administered in 5 days or over a period of many months (13 b). In human trypanosomiasis, as in syphilis, the organisms apparently multiply so slowly that even when injections are administered weekly, there is not sufficient regrowth in the interval between injections to affect the total curative dose significantly as compared with injections repeated daily.

(A different relationship has been observed by Swinyard and Wright (14) in experimental trypanosomal infections of rats, in which repeated small subcurative doses of arsenical were the less effective, the longer the time interval between injections. In that animal, however, there is a fulminating and rapidly fatal infection in which the trypanosomes multiply so rapidly that the volume of organisms in the circulating blood sometimes approaches that of the red blood cells. In such case, and unlike the human disease, the total curative dose is understandably greater the longer the time interval between individual injections.)

It follows from these considerations that, as has proved to be the case in the treatment of syphilis with arsenicals, there is no optimum method for the treatment of human trypanosomiasis with p-arsenosophenylbutyric acid. Provided only that an adequate total amount of the drug is administered, the schedule of injections may, within limits, be adjusted to the convenience of the physician and the patient. Thus, if the treatment "team" is to remain in a given village center until all the population in that area has been surveyed, and until all the cases discovered have completed their treatment, then the duration of treatment is an important consideration. The experience to date indicates that more than 90 percent of early patients may be cured within a period of 2 weeks by daily injections of p-arsenosophenylbutyric acid at 0.5 mg. per kg. to a total of 6 to 7 mg. per kg. There is, moreover, reason to believe that treatment can be completed within 1 week, with almost equal safety, by daily injections at 1 mg. per kg. to the same total dose of 6 to 7 mg. per kg. The compound is however, equally adapted to those plans of treatment in which a mobile "team" travels between three to six treatment centers, remaining in each only long enough to give one injection, and repeating the circuit of those villages for as many times as may be necessary to effect cures. In such case the compound may be injected at 0.5 or 1 mg. per kg. either once weekly, twice weekly, weekly, or even irregularly, to the usual total of approximately 6 to 7 mg. per kg.

There seems to be little to choose between intravenous and intramuscular injection. Both appear to be effective; and against the relative simplicity of the latter procedure is to be weighed the transitory discomfort at the site of injection.

Summary

1. Three hundred and nineteen human cases of early *T. gambiense* infection have been treated with p-arsenosophenylbutyric acid in varying doses, and thereafter observed for varying periods, up to a present maximum of 18 months. These cases, treated with the collaboration of the Sleeping Sickness Services of the Belgian Congo, French Equatorial Africa, French West Africa, the Gold Coast,

Nigeria, and the Firestone Plantation in Liberia represent a reasonable cross section of the disease with respect to age, sex, and geographic distribution. In 221 of these the spinal fluid was known to be normal, and in the remaining 98 it was assumed to be normal on the basis of history and clinical findings.

2. Of the cases known to have been treated in the early stage of the disease, the results varied with the total of drug administered. Thus, at total dosages of 3.5, 3.5 to 4.9, 5.0 to 6.4 and 6.5 or more milligrams per kilogram, the incidence of observed failure to date has been 26, 10, 8, and 4.5, respectively. Although these are crude rates, not corrected for the varying periods of observation, they are believed to represent correct orders of magnitude; and it is estimated that more than 90 percent of the cases can be cured by a total dosage of 6 to 7 mg. per kg.

3. Within the limits of the present experience, the therapeutic efficacy of the compound has been independent of variations in the amount per injection, the number of injections, their frequency, or the total duration of treatment. The important consideration has been solely the total amount of drug received.

4. In 12 patients, intramuscular injections proved as effective as intravenous, and produced only transitory local reaction.

5. Although most of the patients in the present series received an average dose of 0.4 mg. per kg. per injection, as much as 2 mg. per kg. has been injected intravenously daily for 10 days with no untoward effects. The immediate reaction so often observed after the injections of trivalent arsenicals has been conspicuously uncommon, occurring after less than 1 percent of 4,000 injections. Two of the patients died soon after a course of treatment. In one, the physician having left the village, there is no information as to the cause of death. The other is said to have been "possibly a toxic reaction to arsenical."

6. Early infections with *T. gambiense* may be definitively cured within 2 weeks by 12 to 14 daily injections at 0.5 mg. per kg., or within 1 week by 6 to 7 injections at 1 mg. per kg. Where daily injections are not feasible, the same number of injections may be given at any desired interval, up to 1 week apparently, with equal therapeutic efficacy.

7. With the cooperation of the several Sleeping Sickness Services, studies are now in progress on the treatment of advanced cases with central nervous involvement, using p-arsenosphenylbutyric acid alone and in combination with other trypanocidal agents. Studies on animal infestations are also in progress.

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*Public Health Reports (weekly), January-December, vol. 60, Nos. 1 to 52, pages 1 to 1581. 10 cents a number.

*Venereal Disease Information (monthly), January-December, vol. 26, Nos. 1 to 12, pages 1 to 280. 10 cents a number. Title changed to The Journal of Venereal Disease Information, July 1945.

*Journal of the National Cancer Institute (bimonthly), February-June 1945, vol. 5, Nos. 4 to 6, pages 233 to 454; August-December 1945, vol. 6, Nos. 1 to 3, pages 1 to 195. 40 cents a number.

Public Health Engineering Abstracts (monthly), January-November, vol. XXV, Nos. 1 to 11, 32 pages each; index to vol. XXV. (This index takes the place of issue No. 12 of the Abstracts.) No sales stock.

National Negro Health News (quarterly), January-December, vol. 13, Nos. 1 to 4, 24 pages each. No sales stock.

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- 1697. The control of communicable diseases. Report of a committee of the American Public Health Association. (Revised 1945.) 88 pages. 15 cents.
- 2595. Justice and the future of medicine. By Wendell Berge. January 5, 1945. 16 pages. No sales stock.
- 2596. Tularemia: Spontaneous occurrence in the chipmunk. By R. R. Parker. January 5, 1945. 1 page. 5 cents.
- 2597. A study of the complement fixation and Weil-Felix reactions in wild rats as related to the isolation of the virus of endemic typhus. By George D. Brigham and Ida A. Bengtson. January 12, 1945. 18 pages. 10 cents.
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2684. Legislation on hospital surveys, construction, and licensing considered by State legislatures in 1945. By Mary M. Guerin. December 21, 1945. 21 pages. 10 cents.
2685. Notes on compulsory sickness insurance legislation in the States, 1939-44. By Adela Stucke. December 28, 1945. 14 pages. 5 cents.

Supplements to the Public Health Reports

179. The biological, hygienic, and medical properties of zinc and zinc compounds. By D. Mark Hegsted, John M. McKibbin, and Cecil K. Drinker. 1945. 44 pages. 10 cents.
180. Directory of State and Territorial health authorities, 1944. 1945. 16 pages. 5 cents.
181. Formaldehyde—its toxicity and potential dangers. 1945. 9 pages. 5 cents.
182. The notifiable diseases. Prevalence of certain important communicable diseases, by States, 1943. 1945. 12 pages. 5 cents.
183. Toxicity and potential dangers of aerosols and residues from such aerosols containing three percent DDT. (Second report.) By P. A. Neal, W. F. von Oettingen, R. C. Dunn, and N. E. Sharpless. 1945. 32 pages. No sales stock.
184. A comparative study of sampling devices for air-borne micro-organisms. By H. G. duBuy, Alexander Hollaender, and Mary D. Lackey. 1945. 40 pages. 10 cents.
185. Rural water-supply sanitation. Recommendations of the Joint Committee on Rural Sanitation. 1945. 56 pages. 10 cents.
186. The use of DDT in mosquito control. 1945. 96 pages; 8 plates. 20 cents. Also issued in Separates, as follows:

Separate No. 1. DDT investigations at the Henry R. Carter Memorial Laboratory. By S. W. Simmons. 1945. 4 pages. 5 cents.

Separate No. 2. Techniques and apparatus used in experimental studies on DDT as an insecticide for mosquitoes. By S. W. Simmons and Staff. 1945. 20 pages; 6 plates. 10 cents.

- Separate No. 3. Laboratory investigations on the toxicity of DDT residues to adults of *Anopheles quadrimaculatus*. By R. W. Fay, S. W. Simmons, and J. M. Clapp. 1945. 16 pages. 5 cents.
- Separate No. 4. The evaluation of DDT residual sprays for the control of anopheline mosquitoes in dwellings. By Clarence M. Tarzwell and Harry Stierli. 1945. 16 pages. 5 cents.
- Separate No. 5. Operational procedures and equipment used in the practical application of DDT as a residual house spray. By H. Stierli, S. W. Simmons, and C. M. Tarzwell. 1945. 20 pages; 2 plates. 10 cents.
- Separate No. 6. The experimental use of DDT sprays as mosquito larvicides. By Earl H. Arnold, Frederick F. Ferguson, and William M. Upholt. 1945. 16 pages. 5 cents.
- Separate No. 7. Effects of DDT upon some aquatic organisms other than insect larvae. By James B. Lackey and Mary Louise Steinle. 1945. 12 pages. 5 cents.
- Separate No. 8. The experimental use of DDT in the control of the yellow fever mosquito *Aedes aegypti* (L.). By W. M. Upholt, T. B. Gaines, S. W. Simmons, and E. H. Arnold. 1945. 8 pages. 5 cents.
187. Devices for reducing health department records and reports. By Joseph W. Mountin and Evelyn Flook. 1945. 67 pages. No sales stock.
188. The lecithinase activity of *Clostridium perfringens* toxin. By Emery J. Theriault. 1945. 25 pages. 10 cents.
189. A study of nursing school health practices and a recommended health program for student nurses. By Burnet M. Davis, Robert H. Felix, Charlotte Silverman, and Marion E. Altenderfer. 1945. 22 pages. 10 cents.

Public Health Bulletins

289. Bibliography of industrial hygiene 1900-1943. A selected list. Compiled by Ellen F. Bellingham, J. J. Bloomfield, and Waldemar C. Dreessen. 1945. 95 pages. 20 cents.
290. Carbon monoxide: Its hazards and the mechanism of its action. By W. F. von Oettingen. 1944. 257 pages. 35 cents.
291. A medical study of the effect of TNT on workers in a bomb and shell loading plant. By Rudolph F. Sievers, Alfred H. Lawton, Folke Skoog, Paul A. Neal, and W. F. von Oettingen. Report of fatal case of aplastic anemia. By Robert L. Stump, A. Ralph Monaco, and Rudolph F. Sievers. 1945. 98 pages; 8 half-tones. 25 cents.
292. Health service areas. Requirements for general hospitals and health centers. By Joseph W. Mountin, Elliott H. Pennell, and Vane M. Hoge. 1945. 68 pages. 25 cents.
293. The toxicity of molybdenum. By Lawrence T. Fairhall, Robert C. Dunn, Norman E. Sharpless, and E. A. Pritchard. 1945. 36 pages. 10 cents.

National Institute of Health Bulletin

183. Studies of typhus fever. By N. H. Topping, I. A. Bengtson, R. G. Henderson, C. C. Shepard, and M. J. Shear. 1945. 110 pages. 20 cents.

Miscellaneous Publications

32. Manual for coding causes of illness according to a diagnosis code for tabulating morbidity statistics. 1944. 489 pages. \$1.25.

33. At your service. (A pictorial story of the need for an industrial hygiene program—how the experts help solve troublesome problems of unhealthy environment—and how a plant medical and nursing service can help keep workers well.) 1945. 20 pages. 10 cents.
34. Brucellosis (undulant fever). By Alice C. Evans. 1945. 3 pages. 5 cents.

Cancer Series

2. Breast cancer. 1945. 9 pages. 5 cents.

Annual Report

Annual Report of the Surgeon General of the United States Public Health Service for the fiscal year 1944. 1944. 120 pages. 20 cents.

Unnumbered Publications

- Index to Public Health Reports, vol. 59, part 2, July–December 1944. 1945. 10 pages. 5 cents.
- Index to Public Health Reports, vol. 60, part 1, January–June 1945. 1945. 14 pages. 5 cents.
- Index to Journal of the National Cancer Institute, vol. V, August 1944–June 1945. 1945. 9 pages. 5 cents.
- Foreword to Annual Report of the United States Public Health Service, 1944. By Thomas Parran. 1945. 11 pages. No sales stock.
- National Negro Health Week program. This pamphlet is published annually, usually during March, for community leaders in an effort to suggest ways and means by which interested individuals and organizations may be organized for a concerted and effective attack upon the community's disease problems. Thirty-first observance, April 1–8, 1945. 16 pages. 5 cents; \$2.25 per 100 copies.
- National Negro Health Week leaflet. Thirty-first observance. 1945. 2 pages. 5 cents; \$0.50 per 100 copies.
- National Negro Health Week poster. Thirty-first observance. 1945. 5 cents; \$1 per 100 copies.

Reprints from Venereal Disease Information

234. New cases of syphilis and gonorrhea in States, Territories, possessions, Panama Canal Zone, and cities of 200,000 population and over: Statistical reports for the fiscal years 1943–44 and 1942–43. October 1944. 3 pages. 5 cents.
235. New Jersey's penicillin treatment plan for syphilis and gonorrhea. By J. Lynn Mahaffey and Glenn S. Usher. January 1945. 4 pages. 5 cents.
236. The medical officer and the venereal disease education of the soldier. By Robert Dyar. February 1945. 7 pages. 5 cents.
237. Penicillin serum concentrations in the treatment of gonorrhea by delayed intramuscular absorption. By B. L. Zinnamon and V. P. Seeberg. February 1945. 4 pages. 5 cents.
238. The treatment of neurosyphilis by continuous infusion of typhoid vaccine. By Albert Heyman. March 1945. 8 pages. 5 cents.
239. Serologic survey and venereal disease educational program at the San Francisco County Jail. By Richard A. Koch and Lee Hand. April 1945. 8 pages. 5 cents.

240. A State-wide gonococcus culture service. A system utilizing the mail for transmission of specimens. By Glenn S. Usher and Russell Stein. April 1945. 4 pages. 5 cents.
241. Penicillin in gonorrhea—editorial. Penicillin in the treatment of gonorrhea. Results with six hundred and seventy-five women. By Ruth Boring Thomas and Edda Meyer. Treatment of gonorrhea by a single intramuscular injection of penicillin-oil-beeswax: A cooperative study of 1,060 cases. By C. J. Van Slyke and J. R. Heller, Jr. Accelerated methods of treating gonorrhea in the female with penicillin-wax-oil mixtures. By William E. Graham, Robert B. Greenblatt, and George R. Cannefax. May 1945. 20 pages. 10 cents.
242. Analysis of case-finding methods in community venereal disease control. By Harry Pariser. June 1945. 11 pages. 5 cents.
243. Syphilis control through mass blood testing. By W. H. Y. Smith, Lida J. Usilton, and Martha C. Bruyere. June 1945. 4 pages. 5 cents.
244. Contact investigation as a case-finding instrument. By Albert P. Iskrant. June 1945. 8 pages. 5 cents.
245. Clinical action of penicillin on the uterus. By Herbert M. Leavitt. July 1945. 4 pages. 5 cents.
246. State and Territorial health officers consider the problem of venereal disease control. By J. R. Heller. August 1945. 8 pages. 5 cents.
247. The economic cost of paresis in the United States. By Albert P. Iskrant. August 1945. 10 pages. 5 cents.
248. The significance of the first lapse in outpatient venereal disease clinics. By Frederick G. Gillick, Dorothy Stubbs, and Robert R. Swank. September 1945. 4 pages. 5 cents.
249. The frequency of positive serologic test for syphilis in relation to occupation and marital status among men of draft age. By Lida J. Usilton, Paul T. Bruyere, and Martha C. Bruyere. October 1945. 8 pages. 5 cents.
250. The possibility of predicting the future needs in venereal disease control. A study of the effects of mobilization on the case load in District of Columbia clinics. By George C. Ruhland, Frederick G. Gillick, and Ben D. Chinn. October 1945. 8 pages. 5 cents.
251. U. S. Public Health Service Advisory Committee on Public Education for the Prevention of Venereal Diseases—Report to the Surgeon General. By H. H. Hazen. December 1945. 8 pages. 5 cents.
252. Syphilis among civilians during World War II, January 1, 1942, through June 30, 1943. By Lida J. Usilton. December 1945. 4 pages. 5 cents.

Venereal Disease Bulletins

97. The diagnosis of gonorrhea in women. Collection of material for laboratory examination. By P. S. Pelouze. 1945. 7 pages, illustrated. 5 cents.
98. Requirements of premarital legislation. By Margaret R. Zwally and John F. Mahoney. 1945. 20 pages. 10 cents.

PREVALENCE OF COMMUNICABLE DISEASES IN THE UNITED STATES

May 19-June 15, 1946.

The accompanying table summarizes the prevalence of nine important communicable diseases, based on weekly telegraphic reports from State health departments. The reports from each State for each week are published in the PUBLIC HEALTH REPORTS under the section "Prevalence of disease." The table gives the number of cases of these diseases for the 4 weeks ended June 15, 1946, the number reported for the corresponding period in 1945, and the median number for the years 1941-45.

DISEASES ABOVE MEDIAN PREVALENCE

Poliomyelitis.—The number of cases of poliomyelitis rose from 210 during the preceding 4-week period to 567 during the 4 weeks ended June 15. Of the total number of cases reported, 123 occurred in Texas, 111 in Florida, 66 in Alabama, 49 in California, 23 in Colorado, 20 in Louisiana, 17 in Illinois, and 16 in Oklahoma—75 percent of the cases were reported from those 8 States. Cities reporting the largest numbers of cases since the beginning of the year are: Miami 48 cases, Tampa 26, New Orleans 44, San Antonio 49, and Denver 20 cases. Compared with preceding years the current incidence was 1.9 times the 1945 figure for the same 4 weeks, and 2.4 times the 1941-45 median for this period which was represented by the 1944 incidence (237 cases). Each section except the New England and Middle Atlantic contributed to the increase over 1945, and in all sections except the New England the numbers of cases were considerably above the preceding 5-year medians. In the West South Central section the number of cases (165) was almost 4 times the median; in the East South Central section the number (86) was 8 times the median; in the South Atlantic and Mountain regions the numbers (139 and 30, respectively) were 5 times the median; and in the West North Central section the number of cases (32) was more than 6 times the median. Minor increases only were reported from the other sections. An increase of this disease is normally expected at this season of the year, but the rate of increase during the current period was considerably above the rate during these same weeks in the three preceding years, each of which contained a major epidemic.

Diphtheria.—The incidence of diphtheria continued at a high level. For the 4 weeks ended June 15 there were 1,047 cases reported, as compared with 810 for the corresponding period in 1945 and a 1941-45 median of 703 cases. Each section of the country reported an increase over last year's figures for these weeks and in each section except the

East North Central the number of cases represented an appreciable increase over the 1941-45 median. The largest relative increases occurred in the New England and West North Central sections, with minor increases in all of the other sections. For the country as a whole the current incidence was the highest in this period since 1938 when 1,260 cases were reported.

Measles.—The number of cases (100,093) of measles reported for the current 4 weeks was the highest recorded for this period since 1941 when 111,273 cases were reported. The incidence was more than 5 times that in 1945, and 1.6 times the 1941-45 median. Each section of the country contributed to the increase over the 1945 figures and in each region except the West North Central the number of cases was considerably above the 1941-45 median. In the Middle Atlantic

Number of reported cases of 9 communicable diseases in the United States during the 4-week period May 19-June 15, 1946, the number for the corresponding period in 1945, and the median number of cases reported for the corresponding period, 1941-45

Division	Current period	1945	5-year median	Current period	1945	5-year median	Current period	1945	5-year median
	Diphtheria			Influenza ¹			Measles ²		
United States.....	1,047	810	703	2,562	3,479	3,479	100,093	19,349	62,904
New England.....	37	21	14	3	81	14	14,413	1,786	6,472
Middle Atlantic.....	167	103	94	26	21	23	33,469	3,155	9,869
East North Central.....	136	125	131	106	148	180	18,139	3,309	11,186
West North Central.....	117	83	46	30	48	43	3,519	873	4,496
South Atlantic.....	181	134	108	871	745	895	9,832	607	4,621
East South Central.....	70	45	42	117	112	153	1,652	354	919
West South Central.....	160	154	109	1,185	1,905	1,532	5,852	1,990	2,380
Mountain.....	69	50	50	175	346	346	4,324	982	2,789
Pacific.....	110	95	84	49	73	213	8,893	6,293	6,293
	Meningococcus meningitis			Poliomyelitis			Scarlet fever		
United States.....	419	639	639	566	302	237	9,485	15,512	10,123
New England.....	18	36	36	1	5	5	889	1,720	1,415
Middle Atlantic.....	91	145	145	25	41	14	3,175	4,525	3,213
East North Central.....	73	142	142	33	16	12	2,639	4,234	3,041
West North Central.....	33	64	64	32	1	5	653	1,101	700
South Atlantic.....	50	88	88	139	50	27	690	1,294	552
East South Central.....	47	49	49	86	21	11	197	292	278
West South Central.....	56	56	56	165	128	43	188	353	175
Mountain.....	6	11	11	30	8	6	297	419	419
Pacific.....	45	48	48	55	32	29	757	1,574	731
	Smallpox			Typhoid and paratyphoid fever			Whooping cough ³		
United States.....	37	25	43	321	323	411	7,968	10,203	15,016
New England.....	0	0	0	23	17	23	875	1,154	1,154
Middle Atlantic.....	0	0	0	26	35	56	1,535	1,959	2,484
East North Central.....	12	3	17	22	22	35	1,687	1,100	3,115
West North Central.....	7	14	9	16	8	23	284	255	453
South Atlantic.....	1	2	2	58	61	106	1,365	1,792	1,792
East South Central.....	0	0	7	42	67	47	372	453	622
West South Central.....	1	2	10	82	70	86	863	1,252	1,252
Mountain.....	9	3	4	26	19	15	439	359	576
Pacific.....	7	1	3	26	24	24	548	1,879	1,826

¹ Mississippi and New York excluded; New York City included.

² Mississippi excluded.

section the number of cases was 3.5 times the median and in the New England, South Atlantic, and West South Central sections the numbers were more than twice the respective medians. Minor increases were reported from the other sections.

DISEASES BELOW MEDIAN PREVALENCE

Influenza.—For the 4 weeks ended June 15 there were 2,562 cases of influenza reported. The number was about 70 percent of the number reported for this period in 1944 and also of the 1941-45 median which was represented by the 1945 figure (3,479 cases). The incidence was about normal in the Middle Atlantic, West North Central, and South Atlantic sections, but was relatively low in the other 6 geographic regions.

Meningococcus meningitis.—The number of cases (419) of this disease reported during the current 4 weeks was less than 70 percent of the 1941-45 median (639 cases) for the corresponding 4-week period. In the South Central, Mountain, and Pacific sections the incidence stood at about the 1941-45 median level, but in the North Central and Atlantic Coast sections the incidence was considerably below the seasonal expectancy.

Scarlet fever.—The incidence of scarlet fever continued at a relatively low level, the number of cases (9,485) reported for the current 4-week period being about 70 percent of the number reported for the corresponding weeks in 1945 and 90 percent of the 1941-45 median. The incidence was slightly above the seasonal expectancy in the South Atlantic, West South Central, and Pacific sections, but in other regions the numbers of cases were below the preceding 5-year medians.

Smallpox.—The number of cases (37) of smallpox was higher than the number reported for these same weeks in 1945 but it was lower than the 1941-45 median (43 cases). In both the Mountain and Pacific sections the numbers of cases were about two and one-half times the respective medians, but in all other sections the numbers were below the expected seasonal incidence.

Typhoid and paratyphoid fever.—For the 4 weeks ended June 15 there were 321 cases of these diseases reported, as compared with 323 for the corresponding period in 1945 and a 1941-45 median of 411 cases. The numbers of cases were considerably below the 1941-45 median in the Middle Atlantic, East North Central, and South Atlantic sections, but in all other regions the incidence closely approximated the preceding 5-year medians.

Whooping cough.—The incidence of whooping cough was also relatively low, the number of cases (7,968) being less than 80 percent of the number reported for the corresponding 4 weeks in 1945 and about 55 percent of the 1941-45 median. The situation was favorable in

all sections of the country; each section except the East North Central and Mountain reported fewer cases than occurred during these weeks in 1945, and all sections reported a decline from the 1941-45 median figures.

MORTALITY, ALL CAUSES

For the 4 weeks ended June 15 there were 35,103 deaths from all causes reported to the Bureau of the Census by 93 large cities. The preceding 3-year average for the corresponding weeks was 35,015 deaths. The numbers of deaths were lower than the preceding 3-year average during the first 2 weeks of the 4-week period, but during the third and fourth weeks the numbers were 4.2 and 2.8 percent, respectively, higher than the 1943-45 averages.

INCIDENCE OF HOSPITALIZATION, MAY 1946

Through the cooperation of the Hospital Service Plan Commission of the American Hospital Association, data on hospital admissions among members of Blue Cross Hospital Service Plans are presented monthly. These plans provide prepaid hospital service. The data cover hospital service plans scattered throughout the country, mostly in large cities:

Item	May	
	1946	1945
1. Number of plans supplying data.....	80	81
2. Number of persons eligible for hospital care.....	19,999,085	17,737,698
3. Number of persons admitted for hospital care.....	197,365	165,379
4. Incidence per 1,000 persons, annual rate during current month (daily rate × 365).....	116.2	106.7
5. Incidence per 1,000 persons, annual rate for the 12 months ended May 31, 1946.....	108.8	104.2
6. Number of plans reporting on hospital days.....	28	25
7. Days of hospital care per case discharged during month ¹	8.47	8.07

¹ Days include entire stay of patient in hospital whether at full pay or at a discount.

DEATHS DURING WEEK ENDED JUNE 15, 1946

[From the Weekly Mortality Index, issued by the Bureau of the Census, Department of Commerce]

	Week ended June 15, 1946	Correspond- ing week, 1945
Data for 93 large cities of the United States:		
Total deaths.....	8,782	8,849
Average for 3 prior years.....	8,544	
Total deaths, first 24 weeks of year.....	231,370	225,453
Deaths under 1 year of age.....	690	570
Average for 3 prior years.....	690	
Deaths under 1 year of age, first 24 weeks of year.....	14,811	14,744
Data from industrial insurance companies:		
Policies in force.....	67,204,646	67,368,637
Number of death claims.....	11,718	14,204
Death claims per 1,000 policies in force, annual rate.....	9.1	11.0
Death claims per 1,000 policies, first 24 weeks of year, annual rate.....	10.4	10.9

PREVALENCE OF DISEASE

No health department, State or local, can effectively prevent or control disease without knowledge of when, where, and under what conditions cases are occurring

UNITED STATES

REPORTS FROM STATES FOR WEEK ENDED JUNE 22, 1946

Summary

The incidence of poliomyelitis increased slightly during the week in all of the 9 geographic divisions except the East South Central. A total of 204 cases was reported, as compared with 184 last week and a 5-year (1941-45) median of 116. States reporting currently more than 4 cases are as follows (last week's figures in parentheses): *Increases*—New York 7 (4), Illinois 12 (6), Kansas 7 (4), Florida 34 (25), Louisiana 8 (3), Texas 44 (39), Colorado 11 (10), California 18 (14); *decreases*—Alabama 16 (25), Oklahoma 5 (10). Since March 16 a total of 1,117 cases has been reported, as compared with 718 for the same period last year, 519 in 1944, and 592 in 1943. The total for the year to date is 1,583, as compared with 1,115 for the same period last year and an average of 675 for the corresponding periods of the years 1935-44.

Six cases of smallpox were reported for the week—2 in Missouri, and 1 each in Ohio, Tennessee, Louisiana, and Idaho. To date 248 cases have been reported for the country as a whole (including 68 in Washington and 14 in California), as compared with 240 for the corresponding period last year and a 5-year median of 554.

Of the total of 222 cases of diphtheria reported for the week (last week 256), 26 occurred in Texas, 24 in Pennsylvania, 22 in New York, 19 in California, 11 in Ohio, and 10 each in Maryland and Arizona. The total to date is 8,203 as compared with 6,533 for the corresponding period last year and a 5-year median of 6,178.

Approximately 50 cases of Q fever were reported to have occurred in Amarillo, Tex., during the second and third weeks of March. For the week ended June 15, 6 cases of dengue fever and 4 cases of relapsing fever were reported in Texas.

Deaths recorded during the week in 93 large cities of the United States totaled 8,628, as compared with 8,752 for the preceding week, 9,111 and 8,557, respectively, for the corresponding weeks of 1945 and 1944, and a 3-year (1943-45) average of 8,925. The total for the year to date for these cities is 239,968, as compared with 234,564 for the corresponding period last year.

(1048)

Telegraphic morbidity reports from State health officers for the week ended June 22, 1946, and comparison with corresponding week of 1945 and 5-year median

In these tables a zero indicates a definite report, while leaders imply that, although none was reported, cases may have occurred.

Division and State	Diphtheria			Influenza			Measles			Meningitis, meningococcus		
	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45
	June 22, 1946	June 23, 1945		June 22, 1946	June 23, 1945		June 22, 1946	June 23, 1945		June 22, 1946	June 23, 1945	
NEW ENGLAND												
Maine.....	2	2	0				201	1	69	0	0	0
New Hampshire.....	0	0	9				1 101		5	0	1	0
Vermont.....	0	0	0				225	59	59	0	0	0
Massachusetts.....	8	1	2				1 662	330	676	0	3	9
Rhode Island.....	0	0	0	1			91	18	18	0	1	1
Connecticut.....	1	2	1	1	1	1	484	59	200	1	2	2
MIDDLE ATLANTIC												
New York.....	22	11	13	2	2	2	2 234	170	996	9	14	17
New Jersey.....	9	2	3		4	3	1 404	64	432	2	3	3
Pennsylvania.....	24	9	9				1 109	769	553	9	10	10
EAST NORTH CENTRAL												
Ohio.....	11	1	2	3	2	2	548	45	182	3	3	4
Indiana.....	0	8	3		4	2	143	22	63	2	1	1
Illinois.....	6	1	7	1	4	6	315	335	335	2	17	17
Michigan ¹	4	17	9			1	334	261	345	1	6	6
Wisconsin.....	4	3	1	11	4	9	1 109	100	892	1	2	2
WEST NORTH CENTRAL												
Minnesota.....	5	2	2				67	6	117	2	0	1
Iowa.....	3	2	1				174	39	85	2	1	0
Missouri.....	2	4	2	2	8		71	14	65	1	5	5
North Dakota.....	0	1	1	4	10	4	11	3	13	0	0	0
South Dakota.....	2	0	0				10	5	5	0	0	0
Nebraska.....	4	0	1				68	48	48	1	0	0
Kansas.....	3	3	1	1	1	1	30	40	68	1	2	2
SOUTH ATLANTIC												
Delaware.....	0	0	0				17	3	3	0	0	0
Maryland ¹	10	8	4	4	2	2	540	11	74	2	3	3
District of Columbia.....	0	0	0				91	4	16	2	0	2
Virginia.....	3	6	3	76	35	35	200	22	112	3	1	8
West Virginia.....	2	1	1	2		2	18	1	23	0	2	1
North Carolina.....	6	2	4				138	14	120	0	0	1
South Carolina.....	2	8	1	114	66	80	142	10	40	1	0	1
Georgia.....	5	4	4	3	1	12	60	6	29	0	0	2
Florida.....	3	0	2	2	1	6	32	3	50	1	0	1
EAST SOUTH CENTRAL												
Kentucky.....	1	1	2		1	1	84	17	17	6	3	3
Tennessee.....	4	2	3	16	8	8	96	28	28	6	2	2
Alabama.....	3	6	2	10	14	14	121	1	48	1	5	5
Mississippi ¹	2	8	2							0	1	1
WEST SOUTH CENTRAL												
Arkansas.....	1	4	3	9	1	7	36	33	33	1	3	1
Louisiana.....	3	3	3	1	1	1	55	10	13	4	0	1
Oklahoma.....	0	1	1	4	15	10	32	20	67	1	1	1
Texas.....	26	22	23	366	390	189	545	260	260	6	10	5
MOUNTAIN												
Montana.....	1	0	0	1	3	1	93	5	19	0	0	0
Idaho.....	0	1	0	12			21	3	8	0	1	1
Wyoming.....	1	0	0				10	12	18	0	0	0
Colorado.....	4	1	5	6	18	18	133	13	64	1	0	0
New Mexico.....	3	2	2	2		1	45	6	11	0	1	1
Arizona.....	10	1	1	14	38	38	94	3	34	0	0	0
Utah ¹	0	0	0	2	2	1	104	183	98	1	2	1
Nevada.....	0	0	0		2		1		1	0	0	0
PACIFIC												
Washington.....	1	8	5		4	1	65	180	130	1	3	3
Oregon.....	2	0	1	1	1	3	196	26	54	0	0	3
California.....	19	26	19	7	10	28	1 251	944	944	11	13	13
Total.....	222	184	168	678	655	609	14 611	4 206	8 695	85	122	122
25 weeks.....	8 203	6 533	6 178	187 745	65 502	77 756	601 356	87 745	499 064	3 883	5 275	5 275

¹ Includes delayed reports.

² New York City only.

³ Period ended earlier than Saturday.

Telegraphic morbidity reports from State health officers for the week ended June 22, 1946, and comparison with corresponding week of 1945 and 6-year median—Con.

Division and State	Polio-myelitis			Scarlet fever			Smallpox			Typhoid and para-typhoid fever ¹		
	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45	Week ended—		Median 1941-45
	June 22, 1946	June 23, 1945		June 22, 1946	June 23, 1945		June 22, 1946	June 23, 1945		June 22, 1946	June 23, 1945	
NEW ENGLAND												
Maine.....	0	0	0	7	27	14	0	0	0	0	0	0
New Hampshire.....	0	0	0	7	10	2	0	0	0	0	0	0
Vermont.....	0	0	0	1	4	4	0	0	0	0	0	0
Massachusetts.....	0	0	0	100	179	164	0	0	0	9	0	3
Rhode Island.....	0	0	0	4	5	5	0	0	0	0	0	0
Connecticut.....	2	3	1	17	16	25	0	0	0	0	0	1
MIDDLE ATLANTIC												
New York.....	7	16	6	263	427	219	0	0	0	5	6	7
New Jersey.....	4	2	1	99	77	71	0	0	0	3	3	2
Pennsylvania.....	1	1	1	127	294	141	0	0	0	3	2	4
EAST NORTH CENTRAL												
Ohio.....	2	10	3	145	197	101	1	0	0	0	1	4
Indiana.....	2	0	0	31	31	20	0	1	0	0	1	1
Illinois.....	12	2	3	97	129	87	0	0	0	2	2	4
Michigan ¹	0	1	1	75	167	158	0	0	0	2	5	4
Wisconsin.....	1	0	0	49	86	86	0	0	1	0	0	0
WEST NORTH CENTRAL												
Minnesota.....	1	0	1	34	64	23	0	0	0	1	0	0
Iowa.....	1	1	0	11	20	15	0	2	1	0	0	0
Missouri.....	1	1	1	13	23	22	2	0	0	2	2	1
North Dakota.....	2	0	0	5	3	5	0	0	0	0	4	0
South Dakota.....	0	0	0	6	1	3	0	0	0	0	0	0
Nebraska.....	1	0	0	9	19	9	0	0	0	1	0	0
Kansas.....	7	2	1	15	43	18	0	0	0	0	0	0
SOUTH ATLANTIC												
Delaware.....	0	0	0	1	1	2	0	0	0	0	0	0
Maryland ¹	0	1	0	21	47	29	0	0	0	1	0	2
District of Columbia.....	0	0	0	7	18	8	0	0	0	0	1	0
Virginia.....	0	0	0	23	27	10	0	0	0	1	4	4
West Virginia.....	1	0	0	6	22	17	0	0	0	4	2	3
North Carolina.....	4	0	1	8	27	11	0	0	0	5	0	3
South Carolina.....	1	5	2	1	2	2	0	0	0	3	2	2
Georgia.....	4	5	1	4	11	7	0	0	0	4	11	11
Florida.....	34	2	1	2	2	2	0	0	0	3	0	2
EAST SOUTH CENTRAL												
Kentucky.....	2	0	1	16	22	17	0	0	3	3	5	3
Tennessee.....	0	2	1	15	9	9	1	0	0	6	3	3
Alabama.....	16	8	3	8	6	3	0	0	0	1	5	2
Mississippi ¹	4	1	2	1	12	3	0	0	0	2	3	4
WEST SOUTH CENTRAL												
Arkansas.....	1	0	2	2	7	2	0	0	0	3	7	6
Louisiana.....	8	0	2	6	12	4	1	0	0	6	4	6
Oklahoma.....	5	3	2	3	9	3	0	1	0	1	2	3
Texas.....	44	39	4	14	39	25	0	1	0	15	15	16
MOUNTAIN												
Montana.....	0	0	0	2	6	9	0	0	0	2	1	1
Idaho.....	0	0	0	1	4	4	1	0	0	1	1	1
Wyoming.....	0	0	0	4	6	4	0	0	0	0	0	0
Colorado.....	11	2	1	31	21	21	0	0	0	0	0	2
New Mexico.....	3	0	0	4	7	5	0	0	0	0	2	1
Arizona.....	0	0	1	4	12	12	0	0	0	0	0	1
Utah ¹	1	0	0	13	10	10	0	0	0	0	1	0
Nevada.....	0	0	0	1	3	0	0	0	0	0	0	0
PACIFIC												
Washington.....	2	0	0	16	39	23	0	0	0	0	2	2
Oregon.....	1	0	0	16	11	10	0	0	0	0	1	1
California.....	18	9	7	137	234	129	0	0	0	9	1	6
Total.....	294	116	116	1,482	2,448	1,836	6	5	8	98	99	124
25 weeks.....	1,583	1,115	782	80,891	126,110	91,042	248	240	554	1,448	1,606	2,004

¹ Includes delayed reports.

² Period ended earlier than Saturday.

³ Including paratyphoid fever reported separately, as follows: Massachusetts 8; New York 1; New Jersey 1; Illinois 1; Maryland 1; Georgia 1; Florida 3; Louisiana 2; Texas 2; California 7.

Telegraphic morbidity reports from State health officers for the week ended June 22, 1946, and comparison with corresponding week of 1945 and 5-year median—Con.

Division and State	Whooping cough			Week ended June 22, 1946								
	Week ended—		Median 1941-45	Dysentery			Encephalitis, infectious	Rocky Mt. spotted fever	Tularemia	Typhus fever, endemic	Undulant fever	
	June 22, 1946	June 23, 1945		Ame- bic	Bacil- lary	Un- spec- ified						
NEW ENGLAND												
Maine.....	9	46	22	1			3				1	
New Hampshire.....	3		2								3	
Vermont.....	11	16	18								2	
Massachusetts.....	139	75	96									
Rhode Island.....	21	19	19									
Connecticut.....	26	39	30		1		1				5	
MIDDLE ATLANTIC												
New York.....	136	177	245	19	13		1				9	
New Jersey.....	123	157	157	1								
Pennsylvania.....	78	197	206									
EAST NORTH CENTRAL												
Ohio.....	62	107	168								3	
Indiana.....	38	10	13						2		15	
Illinois.....	107	60	102	3	1		5				16	
Michigan.....	130	56	64		2		1				5	
Wisconsin.....	106	30	123						2		9	
WEST NORTH CENTRAL												
Minnesota.....	9	12	39	2							6	
Iowa.....	77	1	24								20	
Missouri.....	6	15	15			1			2			
North Dakota.....	3	2	13									
South Dakota.....			2									
Nebraska.....	2	3	6									
Kansas.....	31	44	46	1							3	
SOUTH ATLANTIC												
Delaware.....		1	2									
Maryland.....	23	82	82			1		5			1	
District of Columbia.....	9	8	10									
Virginia.....	92	46	103			67		7			1	
West Virginia.....	58	11	23									
North Carolina.....	78	221	184					2	2	2		
South Carolina.....	30	53	53	2	13				1	5		
Georgia.....	16	31	31		2			1		16	2	
Florida.....	40	15	13	2						26		
EAST SOUTH CENTRAL												
Kentucky.....	19	45	52					3	1			
Tennessee.....	36	24	34		6		1	1	2	1	2	
Alabama.....	14	23	40							10		
Mississippi.....									1		1	
WEST SOUTH CENTRAL												
Arkansas.....	10	3	16	5	1				3			
Louisiana.....	18	6	13	1						13	2	
Oklahoma.....	29	22	16				2	1			2	
Texas.....	248	243	248	28	580	40	1		2	36	24	
MOUNTAIN												
Montana.....	12	7	15								1	
Idaho.....	13		7			4		1	1		1	
Wyoming.....	14	2	3									
Colorado.....	27	35	35		1				1		1	
New Mexico.....	26	16	16		1							
Arizona.....	11	23	23			8	1				1	
Utah.....	9	37	67								1	
Nevada.....												
PACIFIC												
Washington.....	22	10	16								1	
Oregon.....	13	13	18			2		1				
California.....	68	321	282	4	2					2	8	
Total.....	2,052	2,364	3,475	69	623	123	17	22	20	111	148	
Same week, 1945.....	2,364			40	488	337	8	14	14	107	132	
Average, 1943-45.....	2,883			67	487	275	9	31	18	70		
25 weeks: 1946.....	47,063			1,017	8,636	2,997	225	154	443	1,265	2,241	
1945.....	62,419			793	10,981	3,097	174	127	360	1,471	2,309	
Average, 1943-45.....	69,507		95,277	795	8,244	2,362	241	159	378	1,204		

¹ Period ended earlier than Saturday.

² 5-year median, 1941-45.

Anthrax: New York 1 case.

Leprosy: California 1 case.

WEEKLY REPORTS FROM CITIES

City reports for week ended June 15, 1946

This table lists the reports from 86 cities of more than 10,000 population distributed throughout the United States, and represents a cross section of the current urban incidence of the diseases included in the table.

	Diphtheria cases	Enecephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
NEW ENGLAND												
Maine:												
Portland.....	0	0	---	0	39	0	0	0	5	0	0	
New Hampshire:												
Concord.....	0	0	---	0	---	0	2	0	0	0	0	---
Vermont:												
Barre.....	0	0	---	0	---	0	0	0	0	0	0	---
Massachusetts:												
Boston.....	3	0	---	0	234	1	9	0	28	0	0	18
Fall River.....	0	0	---	0	44	0	2	0	2	0	0	1
Springfield.....	0	0	---	0	98	0	1	0	7	0	1	8
Worcester.....	0	0	---	0	327	0	6	0	2	0	0	30
Rhode Island:												
Providence.....	0	0	1	0	165	0	0	0	2	0	0	21
Connecticut:												
Bridgeport.....	0	0	---	0	2	0	0	0	1	0	1	3
Hartford.....	0	0	---	0	8	0	0	0	2	0	0	5
New Haven.....	0	0	---	0	51	0	0	0	1	0	1	---
MIDDLE ATLANTIC												
New York:												
Buffalo.....	4	0	---	1	22	0	5	0	7	0	0	6
New York.....	12	1	5	1	591	5	41	2	112	0	0	27
Rochester.....	0	0	---	0	96	0	6	0	35	0	0	2
Syracuse.....	0	0	---	0	2	0	1	0	6	0	0	2
New Jersey:												
Camden.....	0	0	---	0	5	0	0	0	1	0	0	2
Newark.....	0	0	---	0	80	1	0	0	8	0	0	14
Trenton.....	0	0	1	1	73	0	2	0	1	0	0	1
Pennsylvania:												
Philadelphia.....	2	0	---	0	109	0	14	1	35	0	0	14
Pittsburgh.....	0	0	1	1	13	1	5	0	14	0	0	6
Reading.....	0	0	---	0	5	0	0	0	3	0	0	6
EAST NORTH CENTRAL												
Ohio:												
Cincinnati.....	1	0	---	0	19	0	5	0	5	0	0	5
Cleveland.....	0	0	1	0	177	2	4	1	32	0	0	11
Columbus.....	0	0	1	1	6	0	3	0	3	0	0	5
Indiana:												
Fort Wayne.....	0	0	---	0	6	0	0	0	1	0	0	3
Indianapolis.....	0	0	---	1	13	0	1	0	5	0	0	8
South Bend.....	0	0	---	0	---	0	0	0	1	0	0	---
Terre Haute.....	0	0	---	0	20	1	1	0	0	0	0	---
Illinois:												
Chicago.....	0	0	---	1	71	3	24	6	62	0	1	35
Springfield.....	0	0	---	0	3	0	1	0	1	0	0	---
Michigan:												
Detroit.....	2	0	---	0	36	0	10	0	35	0	1	48
Flint.....	0	0	---	0	5	0	2	0	3	0	0	3
Grand Rapids.....	0	0	---	0	34	0	0	0	7	0	0	12
Wisconsin:												
Kenosha.....	0	0	---	0	73	0	0	0	0	0	0	---
Milwaukee.....	1	0	1	1	221	1	0	0	4	0	0	43
Racine.....	0	0	---	0	142	0	0	0	3	0	0	1
Superior.....	0	0	---	0	3	0	0	0	1	0	0	3
WEST NORTH CENTRAL												
Minnesota:												
Duluth.....	1	0	---	0	10	0	0	0	0	0	0	---
Minneapolis.....	3	0	---	0	14	1	5	0	7	0	0	2
St. Paul.....	0	0	---	0	6	1	1	0	7	0	0	1
Missouri:												
Kansas City.....	0	0	---	0	1	0	4	0	4	0	0	8
St. Joseph.....	0	0	---	0	---	0	0	0	2	0	0	---
St. Louis.....	3	0	1	0	72	1	5	0	6	0	0	2

City reports for week ended June 15, 1946—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
WEST NORTH CENTRAL—continued												
Nebraska:												
Omaha.....	0	0	---	0	6	0	2	0	2	0	0	---
Kansas:												
Topeka.....	0	0	---	0	---	0	0	0	0	0	0	6
Wichita.....	0	0	---	0	13	0	6	0	0	0	0	1
SOUTH ATLANTIC												
Delaware:												
Wilmington.....	0	0	---	0	1	0	3	0	1	0	0	1
Maryland:												
Baltimore.....	9	0	---	0	500	2	4	0	11	0	0	18
Cumberland.....	0	0	---	0	1	0	0	0	4	0	0	---
Frederick.....	1	0	---	0	3	0	0	0	0	0	0	---
District of Columbia:												
Washington.....	0	0	---	0	127	1	10	0	7	0	1	10
Virginia:												
Lynchburg.....	0	0	---	0	10	0	0	0	0	0	0	---
Richmond.....	0	0	14	1	49	0	1	0	1	0	1	2
Roanoke.....	0	0	---	0	9	0	0	0	0	0	0	---
West Virginia:												
Wheeling.....	1	0	---	0	---	0	0	0	0	0	0	31
North Carolina:												
Raleigh.....	0	0	---	0	4	0	0	0	0	0	0	---
Wilmington.....	1	0	---	0	6	0	0	0	0	0	0	3
Winston-Salem.....	0	0	---	0	7	0	0	0	1	0	0	12
South Carolina:												
Charleston.....	0	0	---	0	1	0	1	0	0	0	0	1
Georgia:												
Atlanta.....	0	0	---	0	17	0	0	1	1	0	0	---
Brunswick.....	0	0	---	0	2	0	0	0	0	0	0	---
Savannah.....	0	0	---	0	8	0	1	0	0	0	0	---
Florida:												
Tampa.....	2	0	1	0	10	0	0	5	1	0	0	3
EAST SOUTH CENTRAL												
Tennessee:												
Memphis.....	0	0	---	0	26	1	6	1	5	0	1	6
Nashville.....	0	0	---	0	2	0	1	0	1	0	1	1
Alabama:												
Birmingham.....	0	0	---	0	10	0	3	0	1	0	0	1
Mobile.....	0	0	---	0	---	0	1	0	0	0	0	---
WEST SOUTH CENTRAL												
Arkansas:												
Little Rock.....	0	0	---	0	12	0	0	0	0	0	0	---
Louisiana:												
New Orleans.....	*8	0	3	0	*42	9	*7	5	4	0	*2	1
Shreveport.....	0	0	---	0	---	0	3	0	0	0	0	---
Texas:												
Dallas.....	2	0	---	0	7	0	0	3	2	0	0	---
Galveston.....	0	0	---	1	1	0	3	0	1	0	0	1
Houston.....	1	0	---	0	3	0	1	2	2	0	0	1
San Antonio.....	0	0	---	0	3	0	6	3	0	0	0	---
MOUNTAIN												
Montana:												
Billings.....	0	0	---	0	3	0	1	0	0	0	0	---
Great Falls.....	0	0	---	0	18	0	2	0	1	0	0	---
Helena.....	0	0	---	0	1	0	0	0	0	0	0	---
Missoula.....	0	0	---	0	5	0	0	0	0	0	0	---
Colorado:												
Denver.....	4	0	1	0	55	0	1	4	9	0	0	17
Pueblo.....	0	0	---	0	32	0	1	0	0	0	0	1
Utah:												
Salt Lake City.....	0	0	---	0	69	0	3	0	2	0	0	3

*Includes monthly reports from Charity Hospital; figures not used in computing rates.

City reports for week ended June 15, 1946—Continued

	Diphtheria cases	Encephalitis, infectious, cases	Influenza		Measles cases	Meningitis, meningococcus, cases	Pneumonia deaths	Poliomyelitis cases	Scarlet fever cases	Smallpox cases	Typhoid and paratyphoid fever cases	Whooping cough cases
			Cases	Deaths								
PACIFIC												
Washington:												
Seattle.....	3	0	-----	0	39	1	1	1	4	0	1	2
Spokane.....	0	0	-----	0	7	0	1	0	0	0	0	1
Tacoma.....	0	0	-----	0	1	0	0	0	3	0	0	4
California:												
Sacramento.....	0	0	-----	0	33	0	2	0	1	0	0	-----
San Francisco.....	3	0	-----	0	66	1	7	1	10	0	0	1
Total.....	59	1	31	10	4,063	33	231	36	536	0	10	489
Corresponding week, 1945..	74	-----	15	12	1,593	-----	257	-----	1,053	2	11	577
Average, 1941-45.....	51	-----	23	11	3,517	-----	1283	-----	776	1	18	931

¹ 3-year average, 1943-45.

² 5-year median, 1941-45.

* Includes monthly reports from Charity Hospital.

Dysentery, amebic.—Cases: New York 5.

Dysentery, bacillary.—Cases: Providence 1; New York 4; St. Louis 1; Baltimore 1; Charleston, S. C., 5; Memphis 1.

Dysentery, unspecified.—Cases: San Antonio 14.

Rocky Mountain spotted fever.—Cases: Missoula 1.

Tularemia.—Cases: Memphis 1.

Typhus fever, endemic.—Cases: Tampa 1; New Orleans 5; * Galveston 1; Houston 2.

Rates (annual basis) per 100,000 population, by geographic groups, for the 86 cities in the preceding table (estimated population, 1943, 32,559,900)

	Diphtheria case rates	Encephalitis, infectious, case rates	Influenza		Measles case rates	Meningitis, meningococcus, case rates	Pneumonia death rates	Pollomyelitis case rates *	Scarlet fever case rates	Smallpox case rates	Typhoid and paratyphoid fever case rates	Whooping cough case rates
			Case rates	Death rates								
New England.....	7.8	0.0	2.6	0.0	2,530	2.6	52.3	0.0	131	0.0	7.8	235
Middle Atlantic.....	8.3	0.5	3.2	1.9	461	3.2	34.3	1.4	103	0.0	0.0	37
East North Central.....	2.4	0.0	1.8	2.4	504	4.3	31.0	4.3	99	0.0	1.2	108
West North Central.....	14.1	0.0	2.0	0.0	245	6.0	46.3	0.0	56	0.0	0.0	40
South Atlantic.....	23.4	0.0	25.1	1.7	1,264	5.0	33.5	10.0	45	0.0	3.3	136
East South Central.....	0.0	0.0	0.0	0.0	224	5.9	64.9	5.9	41	0.0	11.8	47
West South Central.....	8.6	0.0	8.6	2.9	75	25.8	37.3	37.3	26	0.0	0.0	11
Mountain.....	33.0	0.0	8.3	0.0	1,512	0.0	66.1	33.0	99	0.0	0.0	173
Pacific.....	19.6	0.0	0.0	0.0	477	6.5	35.9	6.5	59	0.0	3.3	26
Total.....	9.5	0.2	5.0	1.6	652	5.3	37.1	5.8	86	0.0	1.6	79

PLAGUE INFECTION IN ORANGE AND SAN LUIS OBISPO COUNTIES, CALIF.

Plague infection was reported, under date of June 10, to have been proved on June 7 in specimens taken in San Luis Obispo County, Calif., as follows: A pool of 178 fleas received at the laboratory on May 3, taken from burrows 1 mile north of Pozo; a pool of 200 fleas received at the laboratory on April 26, from burrows 2 miles north of Pozo; a pool of 400 fleas received at the laboratory on April 22, taken from burrows 4 miles south and 1 mile east of Atascadero; a pool of

512 fleas from 90 ground squirrels, *C. beecheyi*, received at the laboratory on April 26, from a ranch 2 miles west and 4 miles north of Pozo; a pool of 200 fleas from 16 ground squirrels, *C. beecheyi*, received at the laboratory on April 25, collected 2 miles west of Pozo. Under date of June 17, plague infection was reported proved, on June 12, in a pool of 200 fleas received at the laboratory on May 3, collected from burrows 1 mile north of Pozo, and in a pool of 107 fleas from 7 ground squirrels, *C. beecheyi*, received at the laboratory on April 25 from a ranch 11 miles south and 1 mile west of Santa Ana, Orange County, Calif.

FOREIGN REPORTS

CANADA

Provinces—Communicable diseases—Week ended May 25, 1946.—During the week ended May 25, 1946, cases of certain communicable diseases were reported by the Dominion Bureau of Statistics of Canada as follows:

Disease	Prince Edward Island	Nova Scotia	New Brunswick	Quebec	Ontario	Manitoba	Saskatchewan	Alberta	British Columbia	Total
Chickenpox.....		29		197	232	10	25	30	88	611
Diphtheria.....		5		13	6	5	2	1		32
Dysentery, bacillary.....				5						5
Encephalitis, infectious.....								1		1
German measles.....				38	44		2	15	4	103
Influenza.....		1			6				6	13
Measles.....		65	3	804	659	45	19	191	11	1,797
Meningitis, meningococcus.....									1	1
Mumps.....			1	90	307	69	33	61	149	710
Poliomyelitis.....				1				1		2
Scarlet fever.....		9	10	130	35	11	2	2	20	219
Tuberculosis (all forms).....		4	8	111	46	12	8	84	38	311
Typhoid and paratyphoid fever.....				7	1				12	20
Undulant fever.....					2					2
Veneral diseases:										
Gonorrhea.....	2	13	15	53	84	28	37	63	128	423
Syphilis.....	2	15	4	83	75	11	11	9	56	266
Whooping cough.....				57	80	1		7	3	148

FINLAND

Notifiable diseases—April 1946.—During the month of April 1946, cases of certain notifiable diseases were reported in Finland as follows:

Disease	Cases	Disease	Cases
Cerebrospinal meningitis.....	23	Paratyphoid fever.....	206
Diphtheria.....	788	Poliomyelitis.....	8
Dysentery.....	21	Scarlet fever.....	262
Gonorrhea.....	1,375	Syphilis.....	580
Malaria.....	2	Typhoid fever.....	37

JAMAICA

Notifiable diseases—4 weeks ended June 1, 1946.—During the 4 weeks ended June 1, 1946, cases of certain notifiable diseases were reported in Kingston, Jamaica, and in the island outside of Kingston, as follows:

Disease	Kingston	Other localities	Disease	Kingston	Other localities
Cerebrospinal meningitis.....		1	Puerperal sepsis.....		1
Chickenpox.....	1	24	Scarlet fever.....	1	
Diphtheria.....	1	2	Tuberculosis (pulmonary).....	7	44
Dysentery (unspecified).....		1	Typhoid fever.....	10	119
Erysipelas.....	2		Typhus fever (murine).....	3	
Leprosy.....		3			

REPORTS OF CHOLERA, PLAGUE, SMALLPOX, TYPHUS FEVER, AND YELLOW FEVER RECEIVED DURING THE CURRENT WEEK

NOTE.—Except in cases of unusual incidence, only those places are included which had not previously reported any of the above-named diseases, except yellow fever, during recent months. All reports of yellow fever are published currently.

A table showing the accumulated figures for these diseases for the year to date is published in the PUBLIC HEALTH REPORTS for the last Friday of each month.

Cholera

Indochina (French)—Cochinchina.—For the period May 11–20, 1946, 109 cases of cholera were reported in Cochinchina, French Indochina.

Thailand (Siam).—For the week ended May 25, 1946, 238 cases of cholera, including 18 cases in Bangkok, were reported in Thailand.

Plague

Egypt.—For the week ended June 18, 1946, plague was reported in Egypt as follows: Alexandria, 8 cases, 3 deaths; Suez, 4 cases.

Indochina (French)—Cochinchina.—For the period May 11–20, 1946, 1 case of plague was reported in Cochinchina, French Indochina.

Smallpox

Nigeria.—Smallpox has been reported in Nigeria as follows: Weeks ended—March 16, 1946, 364 cases, 49 deaths; March 23, 1946, 490 cases, 70 deaths; March 30, 1946, 401 cases, 67 deaths.

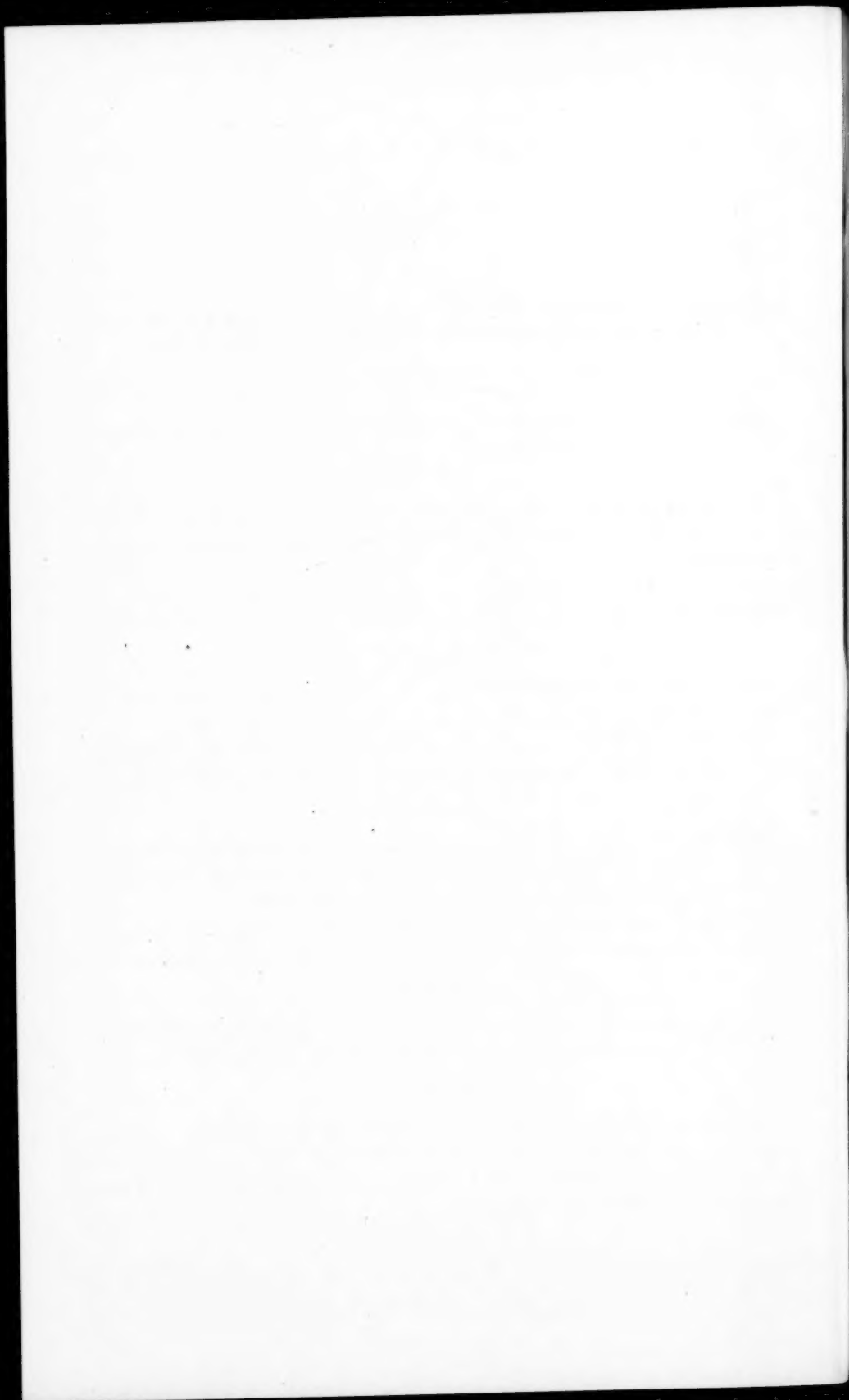
Thailand (Siam).—For the week ended May 25, 1946, 771 cases of smallpox, including 2 cases in Bangkok, were reported in Thailand.

Typhus Fever

Straits Settlements—Malacca.—For the week ended June 15, 1946, 5 cases of typhus fever were reported in Malacca, Straits Settlements.

Yellow Fever

Colombia—Santander Department—Municipality of La Paz—Cachipay.—For the period January 1 to February 28, 1946, 1 death from yellow fever was reported in Cachipay, Municipality of La Paz, Santander Department, Colombia.



FEDERAL SECURITY AGENCY
UNITED STATES PUBLIC HEALTH SERVICE

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DIVISION OF PUBLIC HEALTH METHODS

G. ST. J. PERROTT, *Chief of Division*

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It contains (1) current information regarding the prevalence and geographic distribution of communicable diseases in the United States, insofar as data are obtainable, and of cholera, plague, smallpox, typhus fever, yellow fever, and other important communicable diseases throughout the world; (2) articles relating to the cause, prevention, and control of disease; (3) other pertinent information regarding sanitation and the conservation of the public health.

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